

PRESS RELEASE

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Video available : see end of press release

Geneva, April 11, 2017

The "Geneva Signature" measures the safety and efficiency of a vaccine against Ebola virus disease

An international team based at Geneva University Hospitals (HUG) and at the University of Geneva (UNIGE), Switzerland, has succeeded in defining a "signature" composed of a small number of inflammatory markers that can be monitored in order to understand how a promising anti-Ebola virus vaccine stimulates the immune system. The researchers inoculated 115 volunteers with either a high dose or a low dose of the rVSV-ZEBOV anti-Ebola vaccine, or with placebo. By analyzing the differences between the three groups, they found that it is sufficient to monitor only 5 substances that are naturally present in the blood in order to define immune responses to the vaccine. The "Geneva rVSV-ZEBOV signature" is published in a scientific paper, in *Science Translational Medicine*. It's an easy-to-use equation adding up the concentrations of these 5 substances or markers, most of which are mediated by monocytes, a class of white blood cells known to be active in combatting Ebolavirus in infected individuals. The signature is also expected to inform investigations of safety and immunogenicity of other emerging vaccines.

The 2014–2015 Ebola epidemic affected several countries in West Africa, leading to the death of more than 11'000 people. Although this epidemic of Ebolavirus disease is over, there is no knowing if, when or where another may strike. It is therefore more important than ever to find a reliable vaccine against this deadly disease. Research on vaccines, which was ongoing during the epidemic in West Africa, is now yielding promising results.

Important progress in understanding the vaccine

In an article published on April 12, 2017, in *Science Translational Medicine*¹, a team from the HUG and the UNIGE, working in collaboration with researchers and

¹ Huttner et al., *Sci. Transl. Med.* 9, eaaj1701 (2017) 12 April 2017

clinicians in several other countries in Europe and Africa, has defined a formula that measures the reliability and efficiency of vaccines that might help prevent or limit future outbreaks.

The rVSV-ZEBOV vaccine (recombinant vesicular stomatitis virus–vectored Zaire Ebola vaccine) had already been shown to stimulate the immune system in human volunteers; and in a field trial in 2015 it successfully protected people who had been exposed to Ebola patients from contracting the disease themselves. Yet concerns had been raised during the Geneva trial regarding side effects. What the Geneva team has now published is a detailed examination of the blood plasma of 115 healthy volunteers from Geneva, some of whom received either a low-dose or a high dose of vaccine, while others received a placebo vaccine.

When a vaccine enters the bloodstream, dozens of inflammatory markers that are naturally present see their concentrations change over the next few days. The researchers investigated 15 of them (different varieties of chemokines or cytokines). They found that 1-3 days after the vaccine was administered, the concentration of 6 of these 15 markers had measurably increased. Using a statistical procedure known as principal components analysis, the Geneva team succeeded in producing a simple score that makes the activity of the vaccine much easier to monitor. This "signature" contains only 5 of the 6 markers most likely to change in the presence of the rVSV-ZEBOV vaccine: together, they account for over two-thirds (68%) of the variation in blood cytokine/chemokine activity.

The Geneva Signature found in Gabon

The signature was found to be stronger in volunteers who received the higher dose than in those who got the lower dose.

Importantly, the "Geneva signature" was applied to blood samples from a similar trial that took place in Lambaréné, Gabon, where healthy volunteers had also received the rVSV-ZEBOV vaccine. The same markers were elevated and correlated with side effects and later immunity in the same way.

The 5 markers in the signature are: monocyte attractant protein 1 (MCP-1), the interleukin-1 receptor antagonist (IL-1Ra), tumor necrosis factor (TNF-alpha), interleukin-10 and interleukin-6. Several of these are produced by monocytes or are known to interact with them, so the results imply that monocytes play a critical role in the efficacy and safety of the rVSV-ZEBOV vaccine.

In the case of many other vaccines, such as one recently developed against H1N1 influenza, the chemical markers mostly belong to another category of white blood cells: lymphocytes. Taken together, these signatures help understand how vaccines stimulate the immune system in very different ways to tackle various types of virus. This latest discovery therefore opens up encouraging perspectives for investigating the safety, efficacy and mechanisms of other emerging vaccines.

B-rolls available :

[Interview Dre Angela Huttner, Division of Infectious Diseases at the HUG, co-investigator of the VSV-ZEBOV clinical trial](#)

For further information

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HUG: Care, Teaching and Research

The Geneva University Hospitals (HUG), a reference academic institution at both national and international levels, bring together eight public hospitals and two health clinics. Their centres of excellence cover hepato-biliary and pancreatic diseases, cardiovascular diseases, oncology, musculoskeletal and sports medicine, old age medicine, genetic medicine and vaccinology. With their 10,500 employees, each year the HUG welcome 60,000 patients, offer 990,000 consultations in ambulatory care, and perform 26,000 surgical procedures. More than 800 physicians, 3,000 interns and 150 apprentices are trained at the HUG, which work closely with the Faculty of Medicine of the University of Geneva and the WHO in various training and research projects. Other partnerships include the CHUV, EPFL, CERN and other stakeholders from the Lemanic Health Valley. The annual budget of the HUG is 1.8 billion Swiss francs.

More information on:

- the HUG : www.hug-ge.ch-presse-hug@hcuge.ch
- Activity report, HUG at a Glance, and 2015-2020 Strategic Plan: <http://www.hug-ge.ch/publications-hug>

About the University of Geneva

Founded in 1559 by Jean Calvin and Theodore de Beze, the University of Geneva is the third largest Haute école in Switzerland and is amongst the top 60 best universities in the world. The institution enjoys worldwide recognition and is highly opened to the world. Every year the University welcomes more than 16 000 students in its nine faculties teaching science, medicine, humanities, economics and management, social sciences, law, theology, psychology and educational sciences, translation and interpreting. The University of Geneva has three missions : education, research and knowledge-sharing. The University has been a member of the League of European Research-intensive Universities since 2002. www.unige.ch